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(54) Title: METHODS FOR THE DETERMINATION OF PROTEIN THREE-DIMENSIONAL STRUCTURE EMPLOYING HYDROGEN EXCHANGE ANALYSIS TO REFINE COMPUTATIONAL STRUCTURE PREDICTION

(57) Abstract: The present invention provides methods of structure prediction and/or determination of a protein of interest of unknown structure. Invention methods compare calculated rates of amide hydrogen exchange for a set of predicted possible structures for said protein with experimental hydrogen exchange analysis of said protein to identify valid protein structures based on similarities between hydrogen exchange profiles. In preferred methods, hydrogen exchange analysis is performed by determining the quantity of isotope and/or rate of exchange of peptide amide hydrogen(s) with isotope on a labeled protein, by generating a population of sequence-overlapping endopeptidase fragments of a protein labeled with a hydrogen isotope other than ¹H under conditions of slowed hydrogen exchange, and then deconvoluting fragmentation data acquired from said population of sequence-overlapping endopeptidase-generated fragments.



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